REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 1, 6 and 17 have been amended to more specifically define the binding selectivity of the antibody used in the claimed method. Support is found in the specification at page 14, lines 8-17 and page 15, lines 20-30. Claim 1 has also been amended to more specifically define the assaying method of the immune complex recited in step (C). Support is found in the specification at page 30, lines 20 to page 39, line 21.

Claim 3 has been amended to more specifically define the ratio of binding selectivity of the antibody for the serotype d strain to that for the serotype g strain. Support is found in the specification at page 17, line 27 to page 18, line 6. Claim 4 is deleted without prejudice. Claim 5 is not amended. Claim 6 has been amended in the same manner as claim 1. In addition, claim 6 has been amended to more specifically define the step of preparing the test fluid. Support is found in the specification at page 10, lines 20-25 and page 12, line 20 to page 14, line 3. The amendments to claim 7 are self-explanatory. Claim 8 has been amended in the same manner as claim 3. Claim 9 is cancelled without prejudice. The amendments to claims 10-11 are self-explanatory. Claim 12 is not amended. Claim 13 is cancelled without prejudice. The amendments to claim 14 are self-explanatory. Claims 15 and 16 are amended to more specifically define the immunochromatographic strip according to this invention. Support for the amendments to claim 15 is found in the specification at page 38, line 30 to page 39, line 17 and page 41, lines 13-17. Support for the amendments to claim 16 are found in the specification at page 42, line 9 to page 43, line 10. Claim 17 has been amended in the same manner as claim 1. In addition, claim 17 has been amended to recite a "isolated or purified" polyclonal antibody. Claim 18 has been amended in the same manner as claims 3 and 8.

Turning to the Official Action, claims 1-18 are rejected under 35 USC 112, first paragraph, on the basis of lack of enablement. This ground of rejection is respectfully traversed.

The Examiner indicates that the specification and claims lack deposit information for the deposit of polyclonal antibody α6715. Polyclonal antibody α6715 is, however, readily available to

anyone skilled in the art in reference to the present specification and with use of techniques which are well known in this field. Hence, deposit is considered to have been unnecessary.

Furthermore, the present specification discloses how to obtain polyclonal antibody α6715 of the present invention with use of reference strains which are available to skilled persons. Hence, the Applicants submit that the present application provides an enabling disclosure.

More specifically, it is mentioned in the present specification that the polyclonal antibody of the present invention which is represented by α6715 can be obtained by the immunization of an immune animal with *Streptococcus sobrinus* to obtain a polyclonal antibody against *Streptococcus sobrinus*, and by conducting absorption treatment using cells of *Streptococcus mutans* added at a high proportion of not less than 40 (OD_{600}) to 1 mg of said polyclonal antibody. See the specification at page 20, line 28 to page 21, line 3, and page 24, lines 26-31.

It is further mentioned in the specification that both reference serotype d or g strains (e.g. 2B13, 6715; see the specification, page 21, lines 21-24) which are antigens (*Streptococcus sobrinus* with which immune animals are to be immunized) for obtaining polyclonal antibodies against *Streptococcus sobrinus*, and reference serotype c, e or f strains (e.g., Ingritt, P4, OMZ175; see the specification, page 26, lines 13-15) which are *Streptococcus mutans* to be used for the absorption treatment of polyclonal antibody have long been widely recognized as common reference strains and are being extensively used for various purposes, and are readily available from the place which is mentioned in the specification under the headings of "Materials and methods", "Strains, isolation and cultural conditions" at page 331 of "Ota, F., et al., Zbl. Bakt. Hyg. A265: 330-339, 1972" which is cited in the present specification. See the specification at page 11, lines 7-19.

Accordingly, it is respectfully submitted that the specification is enabling, and reconsideration and withdrawal of this ground of rejection is respectfully solicited.

Claims 1-15 are rejected under 35 USC 112, first paragraph, on the basis of lack of enablement. This ground of rejection is respectfully traversed.

The ground of rejection is summarized as follows:

(i) the present specification does not teach the detection of *Streptococcus sobrinus* when the concentration of *Streptococcus sobrinus* is less than 10^5 cells/ml,

(ii) the specification does not show polyclonal antibodies which fall within the scope of the claims other than α6715, and

(iii) the specification provides no guidance to enable one of ordinary skill to known what kind of antibodies are covered by the claims.

The Examiner states, "Given the lack of guidance contained in the specification and the unpredictability for determining and diagnosing the presence *S. sobrinus*, one of skill in the art could not make or use the broadly claimed invention without undue experimentation."

Applicant, however, does not agree with the Examiner for the following reasons:

As mentioned above, the present specification discloses a method to produce polyclonal antibody which is represented by α6715 (see the specification, page 20, line 28 to page 21, line 3 and page 24, lines 26-31). Anyone skilled in the art would be able to easily produce the polyclonal antibody of the present invention. Whether thus obtained polyclonal antibody satisfies or not the requirement as defined in the claims (i.e., binding ability for *Streptococcus sobrinus* is not less than 100 times that for *Streptococcus mutans*) can be easily confirmed by generally employed ELISA method as mentioned in the present specification, page 15, lines 24-30 without undue experimentation.

Hence, the present specification is described in such a manner as to enable any skilled person to easily produce or use the product or method of the present invention, and, therefore, the present application is considered to meet the requirement of 35 USC 112, first paragraph.

Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully solicited.

Claims 1-18 are rejected under 35 USC 112, second paragraph, as being indefinite for the following reasons.

The Applicant submits that this rejection is overcome by the foregoing amendment to the assaying method of the immune complex. In the amendment, each of the methods (immunoagglutination techniques, optical immunoassay techniques, labeled immunoassay

techniques or a combination thereof) to detect *S. sobrinus* is generally employed in this field, and the principle of measurement for these methods is well known. Furthermore, the specification gives a detailed explanation of these methods. Hence, anyone skilled in the art could easily understand how to use these methods.

Regarding the Examiner's comment set forth in item 6 on page 8 of the Action, it is respectfully submitted that the concern expressed by the Examiner has been overcome by the foregoing amendments.

Regarding the Examiner's comment set forth in item 7 on page 8 of the Action, it is believed that these concerns are also overcome by the amendment to claims 3, 8 and 18 set forth above.

Regarding item 8 on page 9 of the Action, claims 4 and 9 have been cancelled without prejudice. Thus, these concerns have been overcome.

Regarding item 9 on page 9 of the Action, these concerns are believed to be satisfied by the foregoing amendments.

The grounds of rejection are summarized as follows:

(i) the phrase "derived from the saliva and/or dental plaque" is indefinite, and

(ii) the phrase "judging the degree of risk of dental caries" is a relative term, and the risk is not defined in claims.

The Applicants consider that the Examiner's ground (i) is resolved by the foregoing amendment. How to prepare a test fluid using saliva and/or dental plaque is explained in the present specification, at page 10, lines 20-25, and page 12, line 20 to page 14, line 3.

As for the Examiner's ground (ii), the Applicant submits that the phrase is definite for the following reasons.

The term "risk of dental cares" means the possibility of a future occurrence of caries. Epidemiological investigations have clarified that a person who has *S. sobrinus* is liable to suffer from caries in the future. See the specification, page 2, lines 21-29. For example, in the document by Hirose et al. (Caries Re. 1993, 27, pp. 292-297; which has already been filed by IDS; a copy of which is attached hereto) cited in the specification, it is clearly mentioned, "The

prevalence of *S. sobrinus* in saliva was more closely associated with future caries activity..." (page 292, Abstract, lines 18-19). Hence, any skilled person can easily understand the meaning of the phrase "risk of dental caries".

The specification concretely shows the relation between the concentration of *S. sobrinus* in a test fluid which has been prepared using saliva and/or dental plaque taken from the oral cavity, and a "risk of dental caries". See, for example, the specification, page 44, Table 1. It is therefore possible to judge a "risk of dental caries" from the concentration of *S. sobrinus* as determined, on the basis of said relation.

Claim 13 was rejected to as being unclear, as set forth in item 10 on page 10 of the Action. This ground of rejection is deemed to be overcome by the deletion of claim 13.

Lastly, claims 15 and 16 were held to be unclear for the reasons set forth in item 11 on page 10 of the Action.

With regard to claims 15 and 16, the examiner states that it is indefinite how the sample pad operates, what the labeled antibody binds to, what it is labeling, what will cause the release of the labeled antibody that is temporarily held on the conjugate pad, and how the detection antibody will detect *S. sobrinus*.

The Applicant submits that this rejection is overcome by the foregoing amendments to claims 15 and 16.

Claims 17 and 18 are rejected under 35 USC 101 for the reasons set forth in item 12.

This ground of rejection is deemed to be overcome by the foregoing amendments to claims 17 and 18, by the amendments proposed by the Examiner.

Claims 1-13 and 17-18 are rejected under 35 USC 102 as being anticipated Babaahmady et al. This ground of rejection is deemed to be overcome by the foregoing amendments to claims 1 and 6.

Babaahmady et al. which the Examiner has cited as a prior art show, in Table 1, results of analysis of specificity of polyclonal anti-*S. sobrinus* antibody with use of indirect immunofluorescent (IF method). In this Table 1, the evaluation for *S. sobrinus* is "4+", and the evaluation for *S. mutans* c, e, f and h is "-". These analytical results are however visual, and

therefore qualitative, evaluation, and do not directly show that S/M binding selectively as defined in the present invention is not less than 100.

The IF method is conducted with the concentration of antibody arranged so that the specificity of antibody may become maximum (in other words, dilution rate is optimized). Hence, even when antibody having cross reactivity with regard to plural strains is used, strains can be distinguished if only reactivity is different. This is clearly seen from the following points ① and ②:

① Table 1 of Babaahmady et al. shows that anti-mouse FITC, a labeled antibody, has reactivity with strains (e.g., Staph. aureus, M. mucilaginosus, Bifidobacterium dentium, etc.). Since, in IF method labeled antibody is added in the specificity analysis of any antibody, the same fluorescence intensity as exhibited by single use of said labeled antibody must be observed with respect to strains with which said labeled antibody is reactive. In results of analysis of specificity of anti-*S. mutans*, anti-*L. acido-philus* and anti-*L. casei*, the evaluation is "-" with regard to strains with which anti-mouse FITC is reactive.

② Table 3 (page 25 of Bush et al. (Caries Res. 1990: 24, pp. 23-29, a copy of which is attached hereto for your information) cited by Babaahmady et al. show results of study of cross reactivity of anti-*S. mutans* antiserum. Reactivity is, however, different between 1:100 dilution and 1:200 dilution. For example, the evaluation for *S. sobrinus* 6715-WT is "1+" in the case of 1:100 dilution, but, in 1:200 dilution, the evaluation is "0".

S/M binding selectivity in the present invention, on the other hand, is defined as the amount of *S. sobrinus* in comparison with that of *S. mutans* when one and the same amount of antibody is made to react with *S. mutans* and with *S. sobrinus* in such a manner that the same reaction value may be given. Thus, S/M binding selectivity is hardly susceptible to the influence of concentration of antibody, and therefore makes an index for essential cross reactivity.

Since anti-*S. sobrinus* antibody as mentioned in Babaahmady et al. is unavailable, S/M binding selectivity of ths antibody cannot be directly determined. As explained below, however, it is unthinkable that S/M binding selectivity of said antibody is 100 or more.

Since *S. sobrinus* and *S. mutans* have a protein antigen in common, it is usually unthinkable that polyclonal antibody which is obtained by the immunization of whole cells of *S. sobrinus* has no cross reactivity at all with regard to *S. mutans*. It is possible to lower cross reactivity by means of absorption treatment with use of cells which show cross reactivity. As mentioned in the present specification, however, after polyclonal antibody against *S. sobrinus* has undergone absorption treatment with use of *S. mutans* under normal condition, S/M binding selectivity of thus treated polyclonal antibody is at most 26 (see the English text, page 4, lines 6-30).

In the present invention, polyclonal anti-*S. sobrinus* antibody is subjected to absorption treatment with *S. mutans* in such a large amount as is usually not employed in absorption treatment, and, thus, S/M binding selectivity as high as 100 or more has been successfully achieved.

According to Babaahmady et al., the above-mentioned polyclonal anti-*S. sobrinus* antibody is not subjected to absorption treatment with *S. mutans* when prepared (this document does not mention that said polyclonal antibody was subjected to absorption treatment, nor does Bush et al. document which is cited Babaahmady et al. with regard to preparation method have any mention of absorption treatment), and, therefore, it is unthinkable that S/M binding selectivity of polyclonal anti-*S. sobrinus* antibody of Babaahmady et al. is 100 or more.

As stated above, Babaahmady et al. have no mention of S/M binding selectivity of polyclonal anti-*S. sobrinus* antibody. Also from the preparation method for said polyclonal antibody, it is unthinkable that S/M binding selectivity of polyclonal anti-*S. sobrinus* antibody is 100 or more.

Such being the case, the invention of claims 1-13 and 17-18 of the present application is not disclosed in Babaahmady et al., and, therefore, has novelty over Babaahmady et al.

Lastly, claims 15 and 16 are rejected under 35 USC 103 as being unpatentable over Sommer in view of Babaahmady et al. This ground of rejection is believed to be overcome by the foregoing amendments to claims 15 and 16.

The largest characteristic feature of the immunochromatographic strip of claims 15 and 16 is the use of an anti-*S. sobrinus* antibody whose S/M binding selectivity is not less than 100.

As mentioned above, Babaahmady et al. fails to disclose, or suggest, such an antibody and a process for the production thereof. Hence, the invention of claims 15 and 16 is considered to be unobvious over Sommer which teaches immunochromatographic strips in view of Babaahmady et al.

In view of the foregoing, it is believed that each ground of objection and rejection set forth in the Official Action have been overcome. Accordingly, favorable reconsideration and allowance is respectfully solicited.

Respectfully submitted,

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